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Research Collaborations: Trial, Trust, and Truth

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Successful advances in biomedical research increasingly require multigroup collaborations and publication of results in multiauthored papers. It is essential to consider at the outset how to maximize the value of such collaborations while avoiding potential pitfalls.

It is becoming more and more challenging to generate major research contributions as new layers of complexity are continually added to our understanding of basic biological processes. Input from diverse specialties and emerging technologies is increasingly necessary for promoting new discoveries and for providing definitive tests of hypotheses. The National Institutes of Health (NIH) and some other funding agencies provide substantial support for Program Projects, which subsume the research efforts of multiple participating laboratories. A natural consequence of this trend is that major publications frequently involve many contributors from a variety of different laboratories and institutions; there may be over a dozen authors on the scientific publication, and the list includes participants who do not know each other. In fact, some may not even be cognizant of the research specialties and expertise of each of the other coauthors. If all goes well, the potential outcome of these large enterprises may be phenomenal and science will be advanced. But how can quality control be ensured for such large collaborative research ventures? Who is ultimately responsible for ascertaining that every contributor's work is reliable? In scientific research, as in every other human endeavor, there is always the possibility of individual carelessness or lack of competence, unintentional bias, various degrees of plagiarism, and, although exceedingly rare, even falsification of results (Powell, 2006). The senior author or team leader, who has presumably orchestrated the collaborative enterprise, must ultimately assume overall responsibility for the published product of the research, even though that individual may have no direct control or oversight of the activities in each of the contributing research laboratories, or of each participating group leader or student. This person must determine how the responsibilities will be shared among the different groups and how accountability will be assigned (Shamoo and Resnik, 2003). In this Commentary, I offer some suggestions that should not only render the collaborative experience more fulfilling for each of the participants but also should help to ensure that the outcome of the work constitutes reliable science.

Critical elements in carrying out a collaboration should include a *trial* period for the collaborating research groups to establish effective interactions in preliminary studies, efforts to establish *trust* in the competence and reliability of the respective contributors, and ultimately verification of the *truth* of the results and the validity of the conclusions based upon them. The discussion that follows is not meant to be an exhaustive treatment of the complexities of collaborative research. There are a number of sources of detailed information, including a section on "Collaborative Research" within the website of the NIH's Office of Research Integrity (ORI; http://www.ori.dhhs.gov/education/products/niu_collabresearch/collabresearch/crmain.html) and an ORI publication on Responsible Conduct of Research (Steneck and Zinn, 2003).

Choosing Collaborators

There are two fundamentally different approaches to setting up a research collaboration. The collaboration might entail the coalescence of studies already underway in several different laboratories, which are focused upon a common research problem or goal. In that case, the collaboration involves bringing together the different sets of results, usually obtained by complementary approaches (but not necessarily so) and reaching some agreement among participants as to the conclusions to be drawn from the composite study for purposes of a joint publication on the common theme. Alternatively, the project may be initiated in one laboratory and then other individuals or groups are recruited to supply particular input from their own unique specialties. Often this may involve transfer of samples from one laboratory to another for analysis by a specialized procedure, with the results being reported back for incorporation into the fabric of the composite research story. Obviously, the choice of collaborators is an essential first step toward the eventual success of the project. It is important to learn at the outset whether there are any potential conflicts of interest, such as financial interest in commercialization. Other conflicts include those that might

compromise an individual's dedication and impartiality, such as participation in competing collaborations, or involvement in personal relationships that could be interpreted as questionable. Issues of intellectual property and data "ownership" must also be raised for discussion at this early stage.

Early during the negotiations with potential collaborators, the respective roles in the project should be assigned, including the matter of eventual authorship, and the participants' expectations should be stated. Who is responsible for each part of the project and how will the respective contributions be acknowledged in eventual publications? Not everyone who contributes to a research project should necessarily be granted coauthorship on the resulting papers. Every listed author should have contributed substantially to the project with respect to its conception, the design and/or performance of the experiments, the analysis of the results, and/or the drafting of the manuscript describing the project. All authors (and especially students!) should participate in critical reading and approval of the final manuscript submitted for publication. Each author should understand the research problem and should be able to offer an intelligent discussion of the entire project from the perspective of their own involvement in it. There should never be any "courtesy authors," who may have been selected because of previous efforts in this research area or who are considered to add credibility or prestige to the publication (or to themselves), or for any other reason. Those who provide services such as statistical advice or administrative support should not be granted authorship but can be thanked in the acknowledgments. However, there are some gray areas, such as furnishing genetically manipulated organisms, a specially constructed plasmid, or other reagents that have required major effort for their preparation. The last name in the author list should normally be the senior person who takes responsibility for the entire collaborative enterprise. If several research group leaders share that responsibility, then a useful convention is to list them all at the end in some agreed-upon order. The person or persons who carried out most of the actual experiments and their design (often students or postdocs) should be listed first. Some journals now detail the specific contributions from each of the authors at the end of the paper—an excellent initiative that should be broadly promoted.

Building Confidence in the Collaborative Group

Discussions of the entire project should be conducted among the participating groups, and these should occur face-to-face or at least through shared emails or conference phone calls. Decisions need to be made regarding the first set of preliminary experiments. This is not done to immediately test a hypothesis but rather to validate the approaches to be used and to learn their limitations. At this point the participants from the different laboratories should have the opportunity to become acquainted. The questions to be addressed include whether they will be able to work effectively together and whether they have confidence in the integrity of their colleagues. The aggregate of the people in the collaborating groups working in close association should ultimately ensure high standards. It is important to promulgate an attitude of openness with unrestricted challenge and self-criticism in these research discussions to promote the best science. This is especially crucial for the mentoring of students; to the extent that they are drawn into the discussions and encouraged to realize that they are an essential component in the collaborative effort, they will generally mature in a conscientious and responsible manner. When open research discussions are curtailed or short circuited by anyone, that is when one should raise concerns that there may be hidden problems or complications. Again, to the extent that discussions of the research are carried out with the full participation of everyone involved, the development of the project (and the careers of those who participate) will be much more rewarding, and less likely to engender error or misbehavior of any sort. Within the collaboration, the value of individual intuition and insight should not be minimized or ignored. Individuals generate new ideas as grist for committees to elaborate in discussion.

Quality Control in Each Component Group

Careful evaluation of each set of experimental data must be carried out initially within the respective groups working on the collaborative research problem. This should never be relegated to reviewers of an eventual manuscript. Reviewers will rarely have the time to go through each figure with a fine tooth comb for possible evidence of errors in procedures, misrepresentation of data, or falsification of results. Furthermore, reviewers almost never have access to the primary data, so they would generally be unable to recognize problems such as the misuse of graphics-enhancing software. A particular "sin-of-omission" should be noted, and that is the presentation of only a portion of a chromatograph or electrophoretic analysis rather than the entire picture, thereby eliminating potentially important data from a figure. The group leaders must take the lead in this essential self-criticism exercise, but it is useful if representatives from each group meet in conference to provide another level of scrutiny during critical evaluation of the results. The importance of a particular step in a procedure might be overlooked by a collaborator who is not fully familiar with the entire project. The necessity of this detailed level of internal review cannot be overstated. Also, this becomes an opportune time to fully involve students: to obtain their relatively unbiased input and, in so doing, to contribute to their apprenticeship for future careers in research.

Scientists are predominantly motivated by their compulsion to learn the truth. In science, new ideas should

be rigorously challenged and experimental results should be questioned as to their validity and statistical significance. Research scientists are continually designing experiments to challenge and perhaps disprove the hypotheses proposed by their competitive colleagues. Manuscripts submitted to journals are subjected to critical review, hopefully by knowledgeable referees, who may question whether the conclusions are justified by the experimental results and the control data presented. Through these processes every hypothesis is eventually verified or overturned, and the happy outcome is that we achieve a better understanding of the physical basis for the world in which we live. This ongoing process of repeating and checking the data from other researchers and other laboratory groups, if done rigorously, would reduce the chance that anyone would ever contribute falsified or manipulated data.

There are various safeguards to ensure against errors (honest or otherwise) that could arise at multiple stages of the project, beginning with the experimental design and extending through the collection of data and its presentation in figures for publication. Students and postdocs within a laboratory group should be encouraged to scrutinize the findings and critically evaluate the validity of the data obtained by their coworkers. Each group leader should ensure that this is a normal part of mentoring his/her students. But what if a group leader is in fact the originator of misconduct? Then it behooves anyone who is aware of a potential problem to come forth and discuss his or her concerns openly. There should be no stigma attached to being a "whistle-blower"—if there are problems with any aspect of the research it is far better that these are brought to light at the earliest possible opportunity.

How can problems of this sort be avoided or minimized? One obvious approach is to always use "double blind" samples when material is passed to a collaborator for particular analytical procedures. There should be no reason that the collaborator needs to know the identities of the respective coded samples. This simple protocol would also preclude the possibility that even unintentional bias could be introduced into the analysis of "treated" and "control" samples. Indeed, it is important to use blind samples whenever possible, even within an investigator's laboratory, to eliminate unintentional bias. For each procedure, it is also prudent, if possible, to have several people independently carry out the analyses; this might typically involve two postdocs or graduate students, or even the lab director and a student. At the very least, the repetition of an experiment by a student can help to develop confidence in his/her research ability, and if there is a lack of confirmation of the result then this could serve as a didactic challenge to seek the basis for the disagreement. The overall intent must be to ensure that the final product of the research represents the best possible science. Why would anyone want less than that?

Finally, I wish to address the serious issue of the negative impact of one coauthor's carelessness or misbehavior upon the ongoing careers of his/her collaborators and students. Such events can be terribly demoralizing to the coauthors and can even impact the broad public view of a particular area of science. Coauthors become "tainted" by the retractions of published papers, and this may impact their future attempts to publish their research and to receive research grant support. Students may become disillusioned and choose alternative careers. These are gloomy predictions, but they are sufficiently severe that the ethical components of scientific research should be considered well in advance of the possible emergence of a problem. The increased dependence of research upon multilab collaborations has highlighted the need for special attention to approaches for ensuring high-quality science with lasting impact.

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